II. REMARKS

The applicants thank the examiner for indicating that claims 18 and 20-24 define subject matter that is novel and unobvious.

A. Claim Status

Claims 17-29, 31-35, and 37-54 are pending in the application. Claims 1-16 have been previously cancelled. Claims 30 and 36 are cancelled by this amendment. Claims 17, 18, 40, 42, 43 and 44 are amended to correct minor grammar errors, to delete the term "enzyme" from claims that depended from claims that exclude enzymes, and to substitute the recitation "evaporating" for the recitation "forming," as suggested by the examiner. These amendments are editorial in nature and do not present new mater. Claims 17, 28 and 32 are amended to incorporate limitations of claims 18, 30 and 36, respectively. Claims 19-25 and are amended to change their dependency from claim 17 to claim 45. Claims 27-29 and are amended to change their dependency from claim 26 to claim 46

Claims 45-54 are added as new claims. The new claims are fully supported by the original specification as discussed in the section entitled "Support for New Claims." No new matter is introduced by this amendment.

B. Formal Matters Noted in the Office Action

In numbered item 1, the examiner indicates that the appropriate maintenance fee for the U.S. Patent No. 5,098,893 have been paid and therefore the reissue procedures are available for this patent. The paragraph requires no further comment.

In numbered item 2, the examiner objects to this application under 37 CFR 1.172 (a) as lacking the written consent of all assignees owning an undivided interest in the patent.

In reply, the applicants respectfully submit that no assent of the assignee is required in this application because an assent of the assignee in compliance with 37 CFR 1.172 and 3.73 consenting to the reissue of U.S. patent 5,098,893, the same underlying US Patent for the instant application, was previously filed in a reissue application 09/270,791. However, to expedite the prosecution, a new assent of the assignee in compliance with 37 CFR 1.172 and

3.73 is filed concurrently with this response.[1]

In numbered item 3, the examiner indicates that the original patent was surrendered during the prosecution of the parent reissue application 09/270,792.

In reply, the applicants note that this paragraph requires no further comment.

In numbered item 4, the examiner (1) reminds the applicants of the continuing duty of disclosure and (2) obligation to timely call to the attention of the office any prior or concurrent proceeding in which patent No. 5,098,893 is or was involved.

In reply, the applicants believe that all material information, including all relevant information regarding related proceedings, have been filed in the parent 09/290,791 application.

C. Item 5 in the Office Action - The Rejections of Claims 17-44 Based on a Defective Reissue Declaration

In numbered item 5, the examiner rejects claims 17-44 under 35 U.S.C. 251 as being based upon a defective reissue declaration. The examiner indicates that the reissue oath/declaration filed with this application is defective because it fails to contain a statement that all errors which are being corrected in the reissue application up to the filing of the oath/declaration arose without any deceptive intention on the part of the applicants. The examiner states that "[w]hile copies of two reissue oath/declarations from reissue application 09/270,791 have been submitted, those oaths/declarations necessarily refer to errors being corrected in that application. A new reissue declaration specifically drawn to errors being corrected in this application is required".

In reply, the applicants respectfully disagree with the examiner's conclusion that the submitted declarations are defective. The oaths/declarations submitted in the parent reissue application No. 09/270,791 do necessarily refer to errors being corrected in that application, and this application is a continuation of the 09/270,791 reissue application, and this application continues to correct the same errors in the original patent referred to in the oaths/declarations submitted in the parent reissue application No. 09/270,791. However, in

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[1]Assent of the assignee is attached hereto.

order to expedite the prosecution of this reissue application, the applicants are submitting a new reissue declaration concurrently herewith.[2]

D. Items 6 and 7 in the Office Action - The Rejections of Claims 21, 31, 37-39, and 41 Under 35 USC 251 for New Matter

In numbered items 6 and 7, the examiner rejects claims 21, 31, 37-39, and 41 under 35 USC 251, stating that:

> The is no original disclosure supporting the exclusion of rennin as is recited in the instant claims 21, 31, 37, 39, and 41. Rennin is not mentioned in the disclosure, and silence in the specification is not support for a negative claim limitation. See Ex parte Grasselli, 231 USPQ 393, aff'd on reconsideration 231 USPQ 395 (Bd. App. 1983). Accordingly, the negative claim limitation in these claims constitute new matter. Claim 38 recites dissolution in an aqueous solution having pH of about 7, which embraces dissolution at slightly acidic pHs. However, there is no original disclosure in the specification of dissolution at slightly acidic pHs, the only pHs recited in the section of the specification cited by Applicants ranging from 7.0 to 7.6. Accordingly, the pH range recited in claim 38 is new matter. [Office Action page 3 line 20 to page 4 line 6.]

1. Reply to the Rejections of Claims 21, 31, 37, 39, and 41

In reply, the applicants respectfully disagree for the following reasons. The examiner rejects claim 17, 26, and 32, from which claims 21, 31, and 37 depend as either anticipated or obvious in view of Shah. The subject matter defined by claims 21, 37, and 39 excludes rennin. The examiner does not reject claims 21, 31, and 37 over Shah because these claims exclude rennin. Moreover, it appears the examiner would reject claims 39 and 41 over Shah, but for the exclusion of rennin.

The applicants conceived of an invention generically applicable to produce storage stability by generating a glassy state. The subject matter defined by claims 21, 31, 37, 39, and 41 generically claims that invention, and specifically excludes rennin only because of the reference to rennin in the Shah reference. The applicants` admit that the specification of this

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[2] Reissue declaration is attached hereto.

application does not mention rennin. However, that does not mean that the applicant's were not in possession of the genus of the inventions claimed by claims 21, 31, 37, 39, and 41, either including or excluding rennin. The applicant respectfully submits that there is no rational basis for a rule of law precluding negative limitations that exclude a species anticipating a generic claim when the reference does not teach the generic utility of the claimed invention. That is the case here. To the extent case law is inconsistent with this reasoning, it should be overruled, with the USPTO's reliance upon Grasselli not withstanding.

Applicants position is supported by members of the patent bar, as indicated by the reasoning in the article by Mr. Harris Pitlick regarding the written description requirement, which was published in the Journal of the Patent Office Society. A copy of the article is enclosed herewith.[3]

2. Reply to the Rejection of Claim 38

In reply, the applicants respectfully disagree for the following reasons. As stated by the examiner, the specification discloses solutions having pH from 7.0 to 7.6. Explicit disclosure of solutions having pH 7.0 and slightly higher that 7.0 clearly provides adequate support for the claimed language "pH of about 7." While the phrase "about 7" is not verbatim disclosed in the original specification, the claimed invention does not have to be described literally in the specification to satisfy the description requirement. The claim language "about 7" is a mere rephrasing of what is explicitly disclosed in the specification. Therefore, the claimed phrase "pH of about 7" does not constitute new matter.

E. Item 8 in the Office Action - The Rejections of Claims 17-25, 40, and 42-44 as Indefinite

In item 8, the examiner rejects claims 17-25, 40, and 42-44 as indefinite, stating that:

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[3] A copy of Pitlick "Looking BEYOND Blazemarks on Trees - It's Time to Revisit the Description Requirement in the Wake of *Warren-Jenkinson*.", 79 JPPTO Society 625-642, (Vol. 79, No. 9 September 1997) is submitted herewith.

> 8. Claims 17-25, 40, and 42-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. There is no antecedent basis in the claims for the phrase "said step of forming" at claim 17, page 3 of the amendment filed February 15, 2002, line 6, and at claim 18, line 1. The only forming mentioned in the independent claim occurs in the dissolving step, however, it is clear that these sections of the claims should be referring to the evaporating step. Claim 40 at line 9 recites that the biologically active material can be an enzyme, and at line 12 recites that the biologically active material can not be an enzyme. Accordingly, it is not clear if enzymes are embraced within the scope of the claim. Claims 42-44 are indefinite for the same reason. [Office action page 4 line 19 to page 5 line 6.]

In response, the applicant amends claims 17 and 18 by substituting the word "forming" by the word "evaporating." The word "evaporating" has direct antecedent basis in step (2) of claim 17.

In further response, the applicants amend claims 40 and 42-44 by deleting the recitation of enzymes on line 9 of each claim, thus excluding enzymes from the scope of claims 40 and 42-44.

F. Item 9 in the Office Action - The Objection to Claim 18

In item 9, the examiner objects to claim 18, stating that:

> 9. Claim 18 is objected to because of the following informalities: At claim 18, lines 1-2, "subatmospheric" should be one word. [Office action page 5 lines 7-8.]

In response, the applicants have amended claim 18 to comply with the examiner's editorial requirement.

G. Items 10-12 of the Office Action - The Provisional Rejections of Claims 26-44 for Obviousness-type Double Patenting

In items 11 and 12, the examiner provisionally rejects claims 26-44 for obviousness-type double patenting, stating that:

11. Claims 26-44 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over all of the claims of co-pending Application No. 09/270,791. [Office action page 5 lines 23-25.]

12. Claims 26-44 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over all of the claims of co-pending Application No. 09/939,688. [Office action page 5, line 9 to page 7, line 5]

In reply, the applicant agrees that the obviousness-type double patenting rejections over co-pending patent applications Nos. 09/270,791 and 09/939,688 are merely provisional rejections because those two applications are still pending. The applicants will consider how to respond to double patenting rejections either when they are not provisional or when this application is otherwise in condition for allowance, i.e., when the issue is ripe for action.

H. **Items 13-14 in the Office Action - The Rejections of Claims 39-43 as Anticipated by Townsend et al.**

The office action states that:

14. Claims 39-43 are rejected under 35 U.S.C. 102(b) as being anticipated by the Townsend et al article. The Townsend et al article teaches lyophilized mixtures comprising RNase (a peptide) and one of Ficoll 70, sucrose, and polyvinylpyrrolidone as protectants of RNase activity. The mixtures are amorphous, which is consistent with their being in a glassy state. For Ficoll 70, for PVP, and for sucrose at pH 10.0 and 6.4, at least 53% of the initial activity is retained after 30 days storage at 45°C, which is consistent with Applicants' claimed retained activity for a longer period of time but at a lower temperature. See, e.g., the Abstract and Figures 4-6. In view of the similarity in the components of the compositions, the compositions' amorphous state, the protectant function of the Ficoll 70, sucrose, and polyvinylpyrrolidone, and the retained activity of the compositions, the compositions of the Townsend et al article are deemed inherently to have the same storage stability and the same T_g claimed by Applicants and are deemed to anticipate the compositions claimed by Applicants. Sufficient evidence of similarity between the compositions of the Townsend et al article and Applicants' claimed compositions is deemed to be present to shift the burden to Applicants to show that their claimed compositions are unobviously different than those of the Townsend et al article. Note that even a patentable difference in the

process of making does not necessarily impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art. [Office action page 8 line 14 to page 9 line 7.]

In reply, the applicants point out (1) that claims 39-41 specifically limit the claimed composition to no more than 4% by weight water and (2) compositions disclosed in the Townsend et al. publication contain about 16% by weight of water (150 moles of residual water per mole of RNase). See page 194, left hand column, first paragraph. Therefore, the applicants submit that Townsend et al. publication does not anticipate the compositions defined by claims 39-41 of the instant application.

The Townsend et al article's dried products disclosed as containing 150 moles of residual water per mole of RNase (i.e., the residual water equals about 16% by weight of the total dried product....) Given significantly higher water content in its samples containing carrier substances disclosed in the Townsend et al. publication, it is more likely than not that Townsend et al.'s samples stored at 45° C were in an amorphous rubbery state, which is a non-glassy state, and which the subject application distinguishes from a glassy state, and therefore that those samples do not anticipate any one of claims 39-43.

I. Item 15 of the Office Action - The Rejections of Claims 26, 28-31 and 43 as Anticipated by Koyama et al.

In item 15, the examiner rejects claims 26, 28-31 and 43, stating that:

15. Claims 26, 28-31 and 43 are rejected under 35 U.S.C. 102(e) as Koyama et al. Koyama et al teach stabilized water-soluble dry solid compositions comprising proteinaceous bioactive substances, for example hormones. Aqueous solutions of the proteinaceous bioactive substances are combined with aqueous solutions a polysaccharide composed mainly of maltotriose units at a ratio of polysaccharide:protein of preferably 1 to 10,000. The weight ratio of the polysaccharide to the substance is at least 0.5, preferably from 1.0 to 10000. The combined solutions are then dried, either by conventional procedures at reduced pressure and a temperature below 30°C, or else by freeze-drying. In one series of examples, greater than 90% of activity is retained after storage at 37°C for one month, which is consistent with Applicants' requirement for at least 53% retained activity after storage for 8 weeks at 25°C. The dry solid can be formed into a tablet. See, e.g., the Abstract; column 2, lines 10-24 and 38-66; Experiment 3; and the Examples.

> In view of the similarity in the components of the compositions and the retained activity of the compositions, the compositions of Koyama et al are deemed inherently to have the same storage stability and T_g claimed by Applicants and are deemed to anticipate the compositions claimed by Applicants. Sufficient evidence of similarity between the compositions of Koyama et al and Applicants' claimed compositions is deemed to be present to shift the burden to Applicants to show that their claimed compositions are unobviously different than those of Koyama et al. Note that even a patentable difference in the process of making does not necessarily impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art. [Office action page 9 line 8 to page 10 line 5.]

In reply, the applicants first note that the Koyama et al. patent does not disclose the actual state of the resulting compositions. It refers to freeze drying for all of its experiments and examples (see column 3 line 44 (experiment 1-A); column 5 line 13 (experiment 2-B); column 5 line 58 (experiment 3); column 6 lines 45-46 (example 1); (column 6 line 63 (example 2); column 7 line 12 (example 3); column 7 line 48 (example 4); column 8 line 12 (example 5); column 8 lines 56-57 (example 6); and column 9 line 37 (example 7)), but it does not disclose any freeze drying conditions.

The examiner concludes that, in "view of the similarity in the components of the composition and retained activity of the compositions, the compositions of Koyama et al. are deemed inherently to have the same storage stability, and Tg claimed by Applicants".

In reply, the applicants point out that this conclusion is inconsistent with the complete teachings of the Koyama et al. patent.

The Koyama et al. patent teaches that stabilizers *other than a polysaccharide mainly composed of maltotriose units* do ***not*** provide desired high stability. See, for example, Table 1 in columns 3-4 (indicating that various possible stabilizers, except for specific polysaccharides do not retain desired activity of the active substance in the dried state.)

The drying conditions of the Koyama et al.'s samples formed from the stabilizers that do not provide storage stability, and the drying conditions of samples containing the polysaccharide mainly composed of maltotriose units that do provide storage stability, are not explicitly stated. However, the clear implication of the Koyama et al. patent's describing the samples containing the polysaccharide mainly composed of maltotriose units as providing an unexpected satisfaction ("unexpectedly satisfying"; column 2 lines 1-2) of the retention

stability requirement is that the drying conditions *were the same* for the failed and the successful stabilizers, implying that those drying conditions were *freeze drying* conditions.

The Koyama et al. patent discloses that ineffective stabilizers ***do not*** provide storage stability when dried under impliedly the same drying conditions (impliedly freeze drying conditions) as Koyama et al.'s inventive polysaccharides. This fact indicates that the Koyama et al.'s drying conditions *did not* result in glassy state compositions. If Koyama et al.'s drying conditions resulted in the glassy state, all of Koyama et al.'s samples would have been stabilized, as taught by Dr. Franks et al. in this application. Failure of Koyama et al.'s ineffective stabilizers to provide storage stability indicates that compositions containing those ineffective stabilizers were not in a glassy state. In particular, ***dextran*** is disclosed in the Koyama et al. patent as an ineffective stabilizer. As disclosed in the Koyama et al patent, compositions stabilized with ***dextran*** retained only 65.3 % and 81.5 % activity after being stored for two months at 37 ^{o}C and 4^{o}C, respectively. In contrast, this application discloses that compositions comprising ***dextran*** as the carrier substance dried according the the method of the invention disclosed in this application exhibit 102% and 91 % activity when stored at 25 ^{o}C for 8 and 10 weeks, respectively. This exceeds activity of the compositions disclosed in the Koyama et al patent stored for the same period of time. This application shows in example 13, in the table in column 13, that dextran is an effective stabilizer when existing in a glassy state composition. This application teaches broadly (column 2 lines 24-29) that it is the existence of the glassy state that is important for storage stability. The only reasonable conclusion to draw from these facts is that Koyama et al.'s dextran containing samples were not in a glassy state. The logical extension of that conclusion is that Koyama et al.'s inventive compositions were dried under the same conditions as Koyama et al.'s dextran samples and therefore had the same residual water concentration, and therefore that those compositions were too high in water concentration to be in a glassy state.

Therefore, the examiner's conclusion that the similarity in the components of the compositions and the retained activity of Koyama et al. inventive compositions is prima facie evidence that those composition were in a glassy state is inconsistent with the entire teachings of the Koyama et al. patent.

Hence, considering all of what Koyama et al. teaches, instead of just what Koyama et

al. teaches regarding the polysaccharide mainly composed of repeating maltotriose units, indicates that the drying conditions used by Koyama et al. did not result in compositions in a glassy state, and indicates that the examiner's conclusion that "similarity in ... retained activity between Koyama et al's products and Applicants' claimed products" is not "evidence that Koyama et al.'s freeze dried material existed in a glassy state."

Accordingly, the anticipation rejections of claims 26, 28-31, and 43 based upon the Koyama et al. patent are improper and therefore should be withdrawn.

J. **Item 16 of the Office Action - The Rejections of Claims 32-34, 36 and 37 for Obviousness over Koyama in View of Applicants' Admission**

The office action states that:

16. Claims 32-34, 36 and 37 are rejected under 35 U.S.C. 103(a) as being obvious over Koyama et al as applied against claims 26, 28-31 and 43 above, and further in view of Applicants' admission of the prior art at column 1, lines 59-62; column 4, lines 57 - 66; and column 5, lines 3-8. Koyama et al do not teach any examples in which conventional drying procedures at reduced pressure and a temperature below 30°C are used. However, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the dried compositions of Koyama et al using conventional drying procedures at reduced pressure and at a temperature below 30°C because as admitted by Koyama et al, such drying procedures are conventional and are suitable for producing Koyama et al's desired products, and because as admitted by Applicants at column 1, lines 59-62, of the application, freeze-drying is costly in capital and energy and is irreproducible. Regardless of the method used to produce the dried compositions of Koyama et al, the dried compositions of Koyama et al would have been expected to have a T_g greater than 20°C because as admitted by Applicants at column 4, lines 59-60, the Tg for maltotriose is 76°C and as admitted by Applicants at column 5, lines 3-8, the T_g for water-soluble or water-swellable synthetic polymers is a function of molecular weight. Accordingly, the T_g for Koyama et al's polysaccharide composed mainly of maltotriose units would have been expected to be even higher than the 76°C for a maltotriose monomer. The T_g for Koyama et al's proteinaceous bioactive substances would also have been expected to be relatively high because the proteins are also water-soluble polymers of relatively high molecular weight. Even if Koyama et al's dried compositions were to contain several percent residual water after drying, in view of Applicants' admitted rule-of-thumb at column 4, lines 63-65, of an approximately 6°C decrease in T_g for each percent of moisture added, the dried

> compositions would still have a T_g greater than 20°C in view of the relatively high T_g of the major components. [Office action page 10 line 6 to page 11 line 7.]

In reply, the applicants respectfully dispute the conclusion that "it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the dried compositions of Koyama et al. using conventional drying procedures at reduced pressure and at a temperature below 30°C." For one thing, Koyama et al. did not indicate in the Koyama et al. patent, that they actually did that.

Moreover, in 1989, there were no non-freeze drying "conventional drying procedures carried out at a reduced pressure and temperature below 30 °C" (quoting the Koyama et al. patent column 2 lines 52-54) used on proteinaceous bioactive compounds. See Second Franks Declaration dated October 2, 2000 and submitted in the parent application S.N. 09/270,791[4]. Hence, what procedure Koyama et al. was referring to is vague.

One of ordinary skill in the art in 1989 reading the Koyama et al. patent would have recognized the non-freeze drying language (column 2 lines 52 - 55) as mere surplusage unsupported by any experimental results or process conditions, and therefore would not have been motivated to dry without freeze drying. Moreover, one of ordinary skill in the art in 1989 would have believed that drying purified biologically active samples without first freezing them would destroy an unacceptably large fraction of their activity. Second Franks Declaration.

Even assuming for the sake of argument one of ordinary skill in the art in 1989 was in fact motivated to dry an aqueous unstable material without freeze drying, there was no teaching suggesting using the degree of drying required to obtain a composition that is in a glassy state when existing at 20° C. Because those skilled in the art did not know that the amount of residual water was significant, it is likely that following Koyama et al.'s suggestion to experiment with non-freeze drying would not have resulted in a glassy state material.

At best, the passage in the Koyama et al. patent's reference to a non-freeze drying process (column 2 lines 52-55) was a motivation to experiment since (1) it did not identify

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[4] A copy of the Second Franks Declaration is attached hereto.

any process conditions relating to the reduced pressure and temperature (e.g., time of reduced pressure and heat energy to be input to maintain temperature above freezing) that would have resulted in a dry solid containing a proteinaceous bioactive substance (Koyama et al. column 1 lines 9-12) and (2) it did not relate those process conditions to what was required to achieve the intended stability. In hindsight, to apply the column 2 lines 52-55 statement would probably have required (1) determining process conditions resulting in reduced pressure while maintaining temperature between freezing and 30 °C, (2) determining a relationship between long term storage stability and those process conditions by long term storage testing, and (3) identifying from the relationship whether, and under what conditions, if any, long term storage stability could be obtained. Merely providing a motivation to experiment is an insufficient legal basis to maintain an obviousness rejection. In re Dow Chemical Co., 5 USPQ2d 1529, 1532 (Fed. Cir. 1988)("The PTO presents, in essence, an 'obvious to experiment' standard for obviousness. However, selective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings. There must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure." Emphasis supplied.) The Koyama et al. patent, at best, provides a motivation to experiment. Therefore, it is not a proper basis for an obviousness rejection.

Moreover, since Koyama et al. did not provide any indication that processing at a reduced pressure and at temperatures between freezing and 30 °C would actually result in a stabilized water soluble dry solid containing proteinaceous bioactive substance, there was no reasonable expectation of success. Both a suggestion to try and a reasonable expectation of success must be present for an obviousness rejection to be maintained. In re Vaeck, 20 USPQ2d 1438 (Fed. Cir. 1991) ("Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. See In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Both

the suggestion *and the reasonable expectation of success must be founded in the prior art*, not in the applicant's disclosure. Id." Emphasis supplied.) The Koyama et al. patent provides at best a motivation to experiment, not a suggestion to try a specified processing procedure. Moreover, it provides no reasonable expectation of success for a non-freeze dried procedure. For both of these reasons, the obviousness rejections based upon the teachings of Koyama et al. are improper and should be withdrawn.

Moreover, for the reasons presented above in the discussions of the anticipation rejections based upon the Koyama et al. patent, the Koyama et al. patent does not inherently disclose a composition that is in a glassy state at 20° C. Even assuming arguendo that the prior art motivated drying aqueous unstable materials without freeze drying, there is no teaching suggesting using the degree of drying required to obtain a composition that is in a glassy state when existing at 20° C. Moreover, the most logical conclusion is that utilizing drying conditions other that freeze drying, one of ordinary skills in the art would aim at obtaining compositions exhibiting properties as close to the properties of the compositions disclosed in the Koyama et al. patent as possible to obtain satisfactory storage stable compositions. Therefore, following teachings of the Koyama et al patent an ordinary artisan would be motivated to obtain compositions that are too high in water concentration to be in a glassy state, as disclosed in the Koyama et al. patent.

Accordingly, the teachings of the Koyama et al. patent neither alone nor in combination with applicants' admission suggest the claimed invention and obviousness rejections of claims 32-34, 36, and 37 based upon the Koyama et al. patent in view of applicants' admission should be withdrawn.

K. Item 17 of the Office Action - The Rejections of Claims 17, 19, 25, 40, 42-44 as Anticipated by Shah

The office action states that:

> 17. Claims 17, 19, 25, 40, 42-44 are rejected under 35 U.S.C. 102(b) as being anticipated by the Shah dissertation. The Shah dissertation teaches combining rennin, an enzyme, with preservatives such as gelatin (a synthetic polymer as well as a water soluble and a water-swellable synthetic polymer), dextran, hydroxyethyl starch, and sucrose (a disaccharide) in an aqueous

> solution and spray-drying the aqueous solution. Spray drier residence time is about 15 seconds. The spray-drying results in a dried product having from 0.5% to 3.5% water. The air temperature at the bottom (exit) of the dryer is 160 ^{O}F (71 ^{O}C). As high as 93% of activity is retained after storage at 37°C for four months, which exceeds Applicants' requirement for at least 53% retained activity after storage for 8 weeks at 25°C. See, e.g., page 42, lines 3-9; pages 98-99; page 169, lines 1-11; and page 172, lines 3-7. Spray drying occurs without sublimation of water, without freezing of water, and without cooling below 20°C, and results in evaporation of liquid water from the sprayed droplets of the aqueous solution to be dried. In view of the similarity in the components of the compositions, the drying procedures, the water contents of the dried compositions, and the retained activity of the dried compositions, the compositions of the Shah dissertation are deemed inherently to have the same T_g and to be in the same glassy state claimed by Applicants and are deemed to anticipate the compositions claimed by Applicants. Sufficient evidence of similarity between the dried compositions of the Shah dissertation and Applicants' claimed compositions is deemed to be present to shift the burden to Applicants to show that their claimed compositions are unobviously different than those of the Shah dissertation. Note that even a patentable difference in the process of making does not necessarily impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art. [Office action page 11 line 8 to page 12 line 8.]

In reply, the applicants amend claim 17 to include limitations of claim 18, since claim 18 was indicated by the examiner as allowable. In addition, the applicants amended claims 40, and 42-22 to exclude enzymes from the scope of the claim as discussed in sub-section E set forth above. In addition, applicants add new claim 45 listing specific types of enzymes. Rennin, which is a subject matter of the Shah dissertation, is a protease enzyme, as evident, for example, from Table 3 and columns 25-26 of the US Patent 4,705,875[5]. Proteases do not fall within the scope of enzymes listed in new claim 45. The Shah dissertation does not teach any other types of enzymes or any other enzyme species.

Accordingly, the anticipation rejections of claims 17, 19, 25, 40, and 42-44 based upon the Shah dissertation should be withdrawn.

New claims 50, 51, 52 and 53 containing limitations similar to claims 40, 42, 43 and 44, respectively, recite specific types of enzymes that do not include proteases.

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[5] A copy of US Patent 4,705,875 is attached hereto.

L. Item 18 of the Office Action - The Rejections of Claims 17, 19, 25, 40, and 42-44 Anticipation by Shah in View of Applicant's Admission

The office action states that:

> 18. Claims 17, 19, 25, 40, and 42-44 are rejected under 35 U.S.C. 102(b) as being anticipated by the Shah dissertation as applied against claims 17, 19, 25, 40, and 42-44 above, and further in view of Applicants' admission of the prior art at column 4, line 66, and column 5, lines 3-8; and further in view of Forsthoff. The dried compositions of the Shah dissertation would have been expected to have a T_g greater than 20°C because as admitted by Applicants at column 4, line 66, the T_g for sucrose is 55°C and as admitted by Applicants at column 5, lines 3-8, the T_g for water-soluble or water-swellable synthetic polymers is a function of molecular weight. Accordingly, the T_g for the Shah dissertation's dried compositions comprising sucrose and minimal amounts of water would have been expected to be about 55°C. The T_g for the Shah dissertation's dried compositions comprising gelatin, dextran, or hydroxyethyl starch and minimal amounts of water would also have been expected to be relatively high because the preservatives are water-soluble polymers of relatively high molecular weight. Forsthoff shows that rennin (i.e. rennet or chymosin) is pharmacologically active (see, e.g., the Abstract). [Office action page 18 lines 9-21.]

In response, the applicants amended claim 17 to include limitations of claim 18, indicated by the examiner as allowable. In addition, applicants amended claims 40, and 42-22 to exclude enzymes from the scope of the claim as discussed in sub-section E set forth above. In addition, applicants introduces new claim 45 listing specific types of enzymes. Rennin, which is a subject matter of the Shah dissertation, is a protease enzyme, as evident, for example, from Table 3 columns 25-26 of the US Patent 4,705,875 attached herewith. Proteases do not fall within the scope of enzymes listed in new claim 45. The Shah dissertation does not teach any other types of enzymes or any other enzyme species.

Accordingly, the teachings of the Shah dissertation neither alone nor in combination with applicants' admission, nor in combination with Forsthoff teach the claimed invention and anticipation rejections of claims 17, 19, 25, 40, and 42-22 based upon the Shah dissertation in view of applicants' admission should be withdrawn.

M. **Item 19 of the Office Action - The Rejections of Claims 26-29, 32-35 and 38 for Obviousness over Shah**

The office action states that:

> 19. Claims 26-29, 32-35 and 38 are rejected under 35 U.S.C. 103(a) as being obvious over the Shah dissertation. Application of the Shah dissertation is the same as in the above rejection of claims 17, 19, 25, 40 and 42-44. The Shah dissertation does not teach Applicants' claimed weight ratios of biologically active material to carrier substance or Applicants' claimed dissolution pH's. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal weight ratios of the rennin and the preservatives and optimal dissolution pH's in the Shah dissertation because weight ratio and pH are art-recognized result-effective variable which are routinely determined and optimized in the chemical arts. [Office action page 13 lines 1-9.]

In response, the applicants respectfully disagree with the conclusion that claims 26-29, 32-35 and 38 would have been obvious in view of Shah. This is because the applicants dispute the examiner's conclusion that "it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal weight ratios of the rennin and the preservatives and optimal dissolution pH's in the Shah dissertation because weight ratio and pH are art-recognized result-effective variables which are routinely determined and optimized in the chemical arts".

Shah does not disclose a step of dissolving which is conducted at pH of about 7, as defined by claims 38 and newly added claim 51. In fact, both the final rennin solutions and the additive solutions were brought to a pH of 5.6 to ensure stable rennin solutions, because the rennin solutions were unstable in water, or at pH of about 7. See, for example Shah page 52 first full paragraph and page 97 last paragraph. Shah explicitly states that the stability of rennin is maximum at pH of 5.6. See page 34 line 8. Therefore, Shah teaches away from using the claimed neutral or slightly basic solutions. Therefore, utilization a pH of about 7 or higher would have been contrary to the teachings of Shah.

In addition, independent claims 26 and 32 have been amended to exclude enzymes, and claim 32 excludes rennin. Claim 38 has been amended to recited specific types of enzymes that do not include protease type enzymes, and, thus, do not include rennin since

rennin is a protease enzyme. See attached US Patent 4,705,875 and discussions in item L above.

New claims 46 and 47 similar to claims 26 and 32, respectively, recite specific types of enzymes that do not include proteases. Claim 48 having similar limitations to claim 38, but does not list enzymes as a material to be stored.

Accordingly, the teachings of the Shah dissertation do not suggest the claimed invention and obviousness rejections of claims 26-29, 32-35 and 38 based upon the Shah's dissertation should be withdrawn.

N. **Support for New Claims 45 - 54**

The following section shows support for claims 45 - 54.

CLAIM NUMBER	CITATION TO SUPPORT IN ORIGINAL PATENT
45. A process of forming a composition which is storage-stable at 20° C, said composition comprising the steps of: (1) dissolving to form an aqueous solution (a) a carrier substance which is water-soluble or water-swellable and (b) at least one material to be stored;	Claims 1 and 12. Column 3 lines 1-13.
(2) evaporating liquid water from said solution to convert said solution into a composition in a glassy state; wherein said composition has the properties that it is storage-stable and exists in said glassy state when at 20° C;	Column 1 and column 2 lines 30-36.
wherein said composition contains no more than 4 percent by weight of water;	Column 2 line 41.
wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C; wherein said at least one material is selected from the group consisting of	Claims 1, 2, and 12. Column 3 lines 1-13.

peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and	
wherein said step of evaporating comprises heating the combined carrier substance and purified biologically active material to a temperature not exceeding 80° C;	Column 6 lines 22-24.
with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.	Column 9, line 14-19, column 11, lines 6-7 and 50-51, column 12 lines 56-69.

46. A glassy state composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said amorphous carrier substance;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C;

Claim 1, and see claim 17 herein.

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 2:1 and about 1:1;

Column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13.

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

Column 9, line 14-19, column 11, lines 6-7 and 50-51, column 12 lines 56-69.

47. A method of rendering a material storage stable at 20° C which material is unstable in aqueous solution at room temperature of 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution

(a) said material and

(b) a carrier substance which

Claim 12.

is water-soluble or water-swellable;

(2) evaporating liquid water from said solution thereby converting said solution into a glassy state composition;

wherein said material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the property that it is storage stable and exists in said glassy state when at 20° C; and

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 1:2 and about 1:1;

Column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13.

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

Column 9, line 14-19, column 11, lines 6-7 and 50-51, column 12 lines 56-69.

48. A method of forming a composition which is storage-stable at 20° C, said composition comprising:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

(2) forming said solution containing said carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce said composition;

See previous claims.

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C; wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and wherein said composition contains no more than 4 percent by weight of water; and wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C; and	
wherein said step of dissolving comprises dissolving in an aqueous solution having a pH of about 7.	Examples 5 at column 10 line 17; example 6 at column 11 line 7; example 7 column 11 lines 30-34; example 8 lines 40-41; example 9 column 11 last line; example 10 column 12 line 23; example 11 column 12 line 40-43; example 12 column 12 lines 56-57 and 60; example 13 column 13 lines 5-7, Column 9, line 14-19, column 11, lines 6-7 and 50-51, column 12 lines 56-69.
with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.	Column 9, line 14-19, column 11, lines 6-7 and 50-51, column 12 lines 56-69.
49. A composition which is storage-stable at 20° C, comprising: (1) a carrier substance which is water-soluble or water-swellable and is in a glassy state; (2) at least one material to be stored which is dissolved in said carrier substance; wherein said composition exists in a glassy state at 20° C;	See previous claims.

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water; and

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

50. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water;

See previous claims.

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

See previous claims

51. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said carrier substance does not comprise maltotriose; and

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

See previous claims

52. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said biologically active material is not freeze stable; and

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

See previous claims.

53. A method of forming a composition which is storage-stable at 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

forming said solution into a glassy state composition by evaporating liquid water;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides,

nucleotides, dimers or oligomers of nucleosides or nucleotide, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said carrier substance does not comprise maltotriose; and

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

See previous claims.

54. A method of forming a composition which is storage-stable at 20° C, said composition comprising:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

(2) forming said solution containing said carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce said composition;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said composition contains no more than 4 percent by weight of water; and

wherein said composition has the

properties that it is storage stable and exists in a glassy state when at 20° C; and

wherein said step of dissolving comprises dissolving in an aqueous neutral or slightly basic solution having a pH of about 7.

Examples 5 at column 10 line 17; example 6 at column 11 line 7; example 7 column 11 lines 30-34; example 8 lines 40-41; example 9 column 11 last line; example 10 column 12 line 23; example 11 column 12 line 40-43; example 12 column 12 lines 56-57 and 60; example 13 column 13 lines 5-7.

O. Conclusion

In view of the foregoing comments, the applicants submit that this application is now in condition for allowance pending resolution of the provisional double patenting rejection issues. The examiner is urged to contact the undersigned by telephone at 703-415-0012 if that will expedite allowance of this application.

Respectfully Submitted,

10/3/02
Date

Richard A. Neifeld, Ph.D.
Registration No. 35,299
Irina S. Zemel, Ph.D.
Registration No. 43,402

31518
PATENT TRADEMARK OFFICE

Neifeld IP Law, PC
Crystal Plaza 1
2001 Jefferson Davis Highway
Suite 1001
Arlington, VA 22202

Tel: 703-415-0012
Fax: 703-415-0013
Email: rneifeld@Neifeld.com

Printed: October 3, 2002 (7:09pm)
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III. APPENDIX

Marked up version of Claims for Amendment in Response to June 3, 2002 Office Action

Claims 1-16. **Cancelled by amendment filed February 19, 2002.**

Claims 17-44. **Claims 17-29, 31-36, and 37-44 currently pending , claims 30 and 36 cancelled by this amendment.**

Rejected over Shah 17. (Amended) A process of forming a composition which is storage-stable at 20° C, said composition comprising the steps of:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

(2) evaporating liquid water from said solution to convert said solution into a composition in a glassy state;

wherein said composition has the properties that it is storage-stable and exists in said glassy state when at 20° C;

wherein said composition contains no more than 4 percent by weight of water;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C;

wherein said at least one material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said step of [forming] <u>evaporating</u> comprises heating the combined carrier substance and purified biologically active material to a temperature not exceeding 80° C <u>while maintaining subatmospheric pressure on the combined carrier substance and purified biologically active material</u>.

Allowable over art of record 18. (Amended) The process of claim 17 wherein said step of [forming] <u>evaporating</u> comprises [maintaining a sub atmospheric pressure on the combined carrier substance and purified biologically active material while] heating the combination to at least 30° C and not exceeding 80° C.

Rejected over Shah 19. The process of claim [17] <u>45</u> wherein said carrier substance comprises a water soluble or water swellable synthetic polymer.

Allowable over art of record 20. (Amended) The process of claim [17] <u>45</u> wherein said purified biologically active material is not an enzyme.

Allowable over art of record 21. (Amended) The process of claim [17] <u>45</u> wherein said purified biologically active material is not rennin.

Allowable over art of record 22. (Amended) The process of claim [17] 45 wherein said purified biologically active material comprises a hormone.

Allowable over art of record 23. (Amended) The process of claim [17] 45 wherein said purified biologically active material comprises immunogloblulin.

Allowable over art of record 24. (Amended) The process of claim [17] 45 wherein said purified biologically active material comprises a blood clotting factor.

Rejected over Shah 25. (Amended) The process of claim [17] 45 wherein said purified biologically active material comprises a pharmacologically active protein.

Rejected over Shah + Admission and Koyama 26. (Amended) A glassy state composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said amorphous carrier substance;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, [enzymes,] enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C;

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 2:1 and about 1:1; and

wherein said biologically active material is not an enzyme.

Rejected over Shah + Admission, and Koyama 27. (Amended) The composition of claim 46 wherein said composition contains no more than four weight percent water.

Rejected over Shah + Admission 28. (Amended) The composition of claim **[26]** 46 wherein said ratio is about 2:1.

Rejected over Shah + Admission, and Koyama 29. (Amended) The composition of claim **[26]** 46 wherein said ratio is about 1:1.

Rejected over Koyama 30. **(Cancelled by this amendment)**

Rejected over Koyama 31. The composition of claim 26 wherein said biologically active material is not rennin.

Rejected over Shah + Admission, and Koyama + Admission 32. A method of rendering a material storage stable at 20° C which material is unstable in aqueous solution at room temperature of 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution

(a) said material and

(b) a carrier substance which is water-soluble or water-swellable;

(2) evaporating liquid water from said solution thereby converting said solution into a glassy state composition;

wherein said material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, [enzymes,] enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the property that it is storage stable and exists in said glassy state when at 20° C; and

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 1:2 and about 1:1; and

wherein said biologically active material is not an enzyme.

Rejected over Shah + Admission, and Koyama + Admission 33. (Amended) The method of claim [32] 47 wherein said weight ratio is about 1:1.

Rejected over Shah + Admission, and Koyama + Admission 34. (Amended) The method of claim [32] 47 wherein said weight ratio is about 1:2.

Rejected over Shah + Admission 35. (Amended) The method of claim [32] 47 wherein said composition contains no more than 4 weight percent water.

Rejected over Koyama + Admission 36. **(Cancelled by this amendment).**

Rejected over Koyama + Admission 37. The method of claim 32 wherein said biologically active material is not rennin.

Rejected over Shah + Admission 38. A method of forming a composition which is storage-stable at 20° C, said composition comprising:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

(2) forming said solution containing said carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce said composition;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said composition contains no more than 4 percent by weight of water; and

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C; and

wherein said step of dissolving comprises dissolving in an aqueous solution having a pH of about 7;

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes; restriction enzymes, oxidase enzymes, and reductase enzymes.

Rejected over Townsend 39. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and is in a glassy state;

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition exists in a glassy state at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water; and

wherein said biologically active material is not rennin.

Rejected over Shah and Townsend 40. (Amended) A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable;

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, [enzymes,] enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water; and

wherein said biologically active material is not an enzyme.

Rejected over Townsend 41. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and
(2) at least one material to be stored which is dissolved in said carrier substance;
wherein said composition has the property that it exists in a glassy state when at 20° C;
wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;
wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;
wherein said composition contains no more than 4 percent by weight of water; and
wherein said biologically active material is not rennin.

Rejected over Shah and Townsend 42. (Amended) A composition which is storage-stable at 20° C, comprising:
(1) a carrier substance which is water-soluble or water-swellable and
(2) at least one material to be stored which is dissolved in said carrier substance;
wherein said composition has the property that it exists in a glassy state when at 20° C;
wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;
wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, [enzymes,] enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;
wherein said biologically active material is not an enzyme; and
wherein said carrier substance does not comprise maltotriose.

Rejected over Shah, Townsend, and Koyama 43. (Amended) A composition which is storage-stable at 20° C, comprising:
(1) a carrier substance which is water-soluble or water-swellable and
(2) at least one material to be stored which is dissolved in said carrier substance;
wherein said composition has the property that it exists in a glassy state when at 20° C;
wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;
wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, [enzymes,] enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and
wherein said biologically active material is not an enzyme and is not freeze stable.

Rejected over Shah 44. (Amended) A method of forming a composition which is storage-stable at 20° C, comprising the steps of:
(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and
(b) at least one material to be stored;
forming said solution into a glassy state composition by evaporating liquid water;
wherein said composition has the property that it exists in a glassy state when at 20° C;
wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;
wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, [enzymes,] enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;
wherein said biologically active material is not an enzyme; and
wherein said carrier substance does not comprise maltotriose.

NEW CLAIMS

45. (NEW) A process of forming a composition which is storage-stable at 20° C, said composition comprising the steps of:
(1) dissolving to form an aqueous solution
(a) a carrier substance which is water-soluble or water-swellable and
(b) at least one material to be stored;
(2) evaporating liquid water from said solution to convert said solution into a composition in a glassy state;
wherein said composition has the properties that it is storage-stable and exists in said glassy state when at 20° C;
wherein said composition contains no more than 4 percent by weight of water;
wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C;
wherein said at least one material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and
wherein said step of evaporating comprises heating the combined carrier substance and purified biologically active material to a temperature not exceeding 80° C;
with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes; restriction enzymes, oxidase enzymes, and reductase enzymes.

46 (NEW). A glassy state composition which is storage-stable at 20° C, comprising:
(1) a carrier substance which is water-soluble or water-swellable and
(2) at least one material to be stored which is dissolved in said amorphous carrier substance;
wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C;

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 2:1 and about 1:1;

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from restriction dehydrogenase enzymes, enzymes, oxidase enzymes, and reductase enzymes.

47. (NEW). A method of rendering a material storage stable at 20° C which material is unstable in aqueous solution at room temperature of 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution

(a) said material and

(b) a carrier substance which is water-soluble or water-swellable;

(2) evaporating liquid water from said solution thereby converting said solution into a glassy state composition;

wherein said material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the property that it is storage stable and exists in said glassy state when at 20° C; and

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 1:2 and about 1:1;

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from restriction enzymes, oxidase enzymes, and reductase enzymes.

48. (NEW.) A method of forming a composition which is storage-stable at 20° C, said composition comprising:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

(2) forming said solution containing said carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce said composition;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of

nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said composition contains no more than 4 percent by weight of water; and

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C; and

wherein said step of dissolving comprises dissolving in an aqueous solution having a pH of about 7;

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

49. (NEW). A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and is in a glassy state;

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition exists in a glassy state at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water; and

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

50. (NEW). A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water;

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

51. (NEW) A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said carrier substance does not comprise maltotriose; and

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

52. (NEW) A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said biologically active material is not freeze stable; and

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

53. (NEW) A method of forming a composition which is storage-stable at 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

forming said solution into a glassy state composition by evaporating liquid water;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotide, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said carrier substance does not comprise maltotriose; and

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

54. (NEW) A method of forming a composition which is storage-stable at 20° C, said composition comprising:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

(2) forming said solution containing said carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce said composition;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said composition contains no more than 4 percent by weight of water; and

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C; and

wherein said step of dissolving comprises dissolving in an aqueous neutral or slightly basic solution having a pH of about 7.

Claims 30 and 36 are cancelled by this amendment.

Printed: October 3, 2002 (7:09pm)
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